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**REMARKS**

After entry of this amendment, claims 1-41 are currently pending in the instant application. Claims 1-22 and 25-41 have been withdrawn. Claims 23 and 24 are under active consideration. Claims 23 and 24 have been amended to correct minor typographical errors. The subject matter of the amended claim recitations is fully supported in the specification. In particular, support for the amended recitation of claim 23 is found in the specification, *inter alia*, Example 2, pages 17-26 and Example 3, pages 26-27. No new matter has been added.

**Title of the Invention**

The Examiner requires a new title that is indicative of the invention to which the claims are directed.

Applicants have amended the title to reflect the subject matter of claims 23 and 24 which are under active consideration.

**Informalities**

Claim 23 is objected to because of the informality of missing the word "method".

Claim 23 has been corrected to recite "A method..." Thus, this objection has been overcome.

**Rejections under 35 U.S.C. § 112**

Claims 23 and 24 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite.

According to the Examiner, claim 23 is indefinite in the recitation of UDD protein without providing a SEQ ID NO for the protein. The Examiner also contends that claim 23 is incomplete for an omitting essential step as to how to monitor or diagnose a chronic inflammatory disease.

Applicants respectfully disagree with this rejection for the reasons detailed below. According to applicable case law, the requirement of 35 U.S.C. § 112, second paragraph, means that the claims must have a clear and definite meaning when construed in the light of the complete patent document. *Standard Oil CO. v. American Cyanamide Co.*, 774 F.2d 448, 227 USPQ 293 (CAFC 1985). The test of definiteness is whether one skilled in the art would understand

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the bounds of the claim when read in light of the specification. *Orthokinetic Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1 USPQ2d 1081 (CAFC 1986).

Claim 23 as presently amended (and claim 24 dependent thereon) recites a method comprising determining a level of a UDD-protein selected from the group consisting of *UCH-L3* and *HC3*. The specification discloses at page 7, lines 6-16, that a UDD-protein is "a class or proteins which mediate ubiquitin-dependent degradation which is characterized in that it is expressed in a macrophage that is hyperactivated according to the invention at a lower or higher level than the control level in a macrophage which is not hyperactivated." The specification also discloses at page 7, lines 18-22 that a UDD-protein according to the present invention is *UCH-L3* (Larsen, C.N. *et al.* (1998) *Biochemistry* 37, 3358-3368), or proteasome subunit *HC3* (Tiao, G. *et al.* (1997) *J. Clin. Invest.* 99, 163-168; Hobler, S.C. *et al.* (1999) *Am. J. Physiol.* 277, R434-R440), depicted in the sequence listing (as SEQ ID NO:4 and SEQ ID NO:8, respectively). Thus, the specification defines the function of a UDD-protein and provides references which indicate that one skilled in the art would know what is meant by a "UCH-L3" and "HC3" protein. In view of the foregoing, Applicants submit that the terms "UCH-L3" and "HC3" as described in the specification meet the requirements for definiteness under Section 112 in that one skilled in the art would clearly understand what is covered by the claim.

With regard to the rejection for omitting an essential step, Applicants point out that step (c) of claim 23, as amended, recites "wherein a difference in the levels of the UDD-protein indicates the presence of a chronic inflammatory airway disease." Applicants submit that in view of the amendments, this rejection under Section 112 has been overcome.

Applicants submit that in view of the amendments and remarks above, all the rejections under Section 112, second paragraph have been overcome and must be withdrawn.

Claims 23 and 24 are rejected under 35 U.S.C. § 112, first paragraph for lack of enablement.

According to the Examiner, the specification, while being enabling for a method for diagnosing or monitoring a chronic inflammatory airway disease comprising determining the levels of UDD-protein consisting of an amino acid sequence of SEQ ID NO:4 or SEQ ID

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NO:8, does not reasonably provide enablement for a method for diagnosing or monitoring a chronic inflammatory airway disease comprising determining the levels of *any* UDD-protein.

Applicants respectfully disagree. Applicants point out that claim 23 as presently amended (and claim 24 dependent thereon) recites a method comprising determining a level of a UDD-protein selected from the group consisting of *UCH-L3 and HC3*. Applicants direct the Examiner's attention to Example 2, pages 17-26 and Example 3, pages 26-27 wherein working examples of methods comprising determining the level of UCH-L3 and HC3, respectively, are provided. Applicants also direct the Examiner's attention to page 7, lines 18-22 of the specification which provides guidance as to what is encompassed by a UCH-L3 and HC3 protein. In view of the detailed teaching and exemplification in the present specification, Applicants submit that the specification provides ample guidance to enable the skilled artisan to practice the claimed invention. Thus, this rejection under Section 112 for lack of enablement has been overcome and must be withdrawn.

Claims 38 and 43-59 [*sic*] are rejected under 35 U.S.C. § 112, first paragraph for lack of written description.

According to the Examiner, while the Applicants are in possession of a method for diagnosing or monitoring a chronic inflammatory airway disease, comprising determining the levels of UDD-protein consisting of an amino acid sequence of SEQ ID NO:4 or SEQ ID NO:8, Applicants are not in possession of a method for diagnosing or monitoring a chronic inflammatory airway disease, comprising determining the levels of *any* UDD-protein.

As a preliminary matter, Applicants point out that claims 23 and 24 are under consideration in the instant application and respond to this rejection accordingly. Applicants respectfully disagree with this rejection and submit that claim 23 as presently amended (and claim 24 dependent thereon) recites a method comprising determining a level of a UDD-protein selected from the group consisting of *UCH-L3 and HC3*. Applicants direct the Examiner's attention to Example 2, pages 17-26 and Example 3, pages 26-27 wherein working examples of methods comprising determining the level of UCH-L3 and HC3, respectively, are provided. Applicants submit that the specification provides ample evidence of possession of the claimed invention. Thus, this rejection under Section 112 for lack of written description has been overcome and must be withdrawn.

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In light of the above amendments and remarks, it is submitted that all the rejections under 35 U.S.C. §112, first and second paragraphs have been overcome and must be withdrawn.

**Rejections under 35 U.S.C. § 102**

Claims 23 and 24 are rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,307,035 ("the '035 Patent") as is evidenced by <http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/I/Inflammation.html.2004> ("the Inflammation reference").

Applicants emphatically disagree with this rejection for the reasons detailed below.

**The Cited References**

**U.S. Patent No. 6,307,035**

According to the Examiner, the '035 Patent teaches a method for monitoring or diagnosing diseases associated with abnormal expression of UDD-protein. The Examiner also asserts that the '035 Patent teaches a UDD-protein of SEQ ID NO:18 that is 100% identical to the claimed UDD-protein of SEQ ID NO:4. In addition, the Examiner contends that the '035 Patent teaches that abnormal expression of UDD-protein is associated with various diseases, including lung cancer.

**The Inflammation Reference**

According to the Examiner, the Inflammation reference teaches that chronic inflammatory airway diseases, including chronic bronchitis and COPD are frequent causes of lung cancer, thus a method taught by the '035 Patent would inherently diagnose or monitor a chronic inflammatory airway disease.

**Novelty of the Present Claims**

Claim 23 as presently amended (and claim 24 dependent thereon) recites a method for diagnosing or monitoring a *chronic inflammatory airway disease* comprising determining a level of a UDD-protein selected from the group consisting of UCH-L3 and HC3. Applicants respectfully submit that chronic inflammatory airway disease is not an essential preliminary stage of lung cancer; thus, lung cancer does not anticipate chronic inflammatory airway disease.

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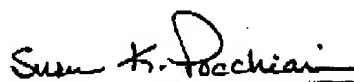
By way of analogy, Applicants submit that there are many ways that a car becomes broken so that one cannot drive it anymore. For example, one way can be that the rubber and plastic material in the engine crumbles, another way can be that the chassis has been smashed by a car accident, a further way can be that the car just rusts. If one way is disclosed to prevent a car from being broken by preventing the rubber and plastic material to become crumbled, this does not anticipate a method for preventing rust. Applicants submit that there are many ways to develop lung cancer. Thus, chronic inflammatory airway disease is not the sole preliminary stage of lung cancer. Because chronic inflammatory airway disease is not an essential preliminary stage of lung cancer, lung cancer does not anticipate chronic inflammatory airway disease.

In view of the above remarks, Applicants submit that this rejection under Section 102 has been overcome and must be withdrawn.

#### CONCLUSION

In light of the above amendments and remarks, Applicants submit that all of the objections and rejections have been overcome and must be withdrawn. Further, Applicants submit that the application is now in form for issuance and an early allowance is earnestly requested. If any issues remain, the Examiner is invited to telephone the Attorney at the number below.

Respectfully submitted,



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